

Cognitive Remediation in Schizophrenia

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Abstract

It is well established that many people with a diagnosis of schizophrenia experience significant problems with thinking skills such as concentration, memory, comprehension of social information, reasoning, and organization. These are often experienced by the individuals themselves as debilitating and demoralizing, but crucially, they also can limit people in their capacity to achieve fundamental life goals, such as working, having fulfilling relationships and living independently, which underpin well-being and a satisfactory quality of life. Cognitive remediation for schizophrenia is a psychological therapy that aims to improve thinking skills and consequently to benefit other more general areas of functioning and improve quality of life.

This entry will summarize the foundational research background to the development and effectiveness of cognitive remediation; and the cutting-edge research into the developments in our understanding of the mechanisms of cognitive change and its relationship to improvements in everyday functioning, and new applications for cognitive remediation. The key aims for the field of cognitive remediation are now (i) to optimize its effectiveness in improving cognitive skills, but critically, in a way that ensures that these cognitive improvements have a measurable impact on other more general life skills, and (ii) to facilitate the wider dissemination of cognitive remediation into the clinical community. To achieve these goals, we need to establish an evidence-based, theoretical underpinning to cognitive remediation, including an understanding of the active ingredients and how best to deliver the therapy.

INTRODUCTION

A diagnosis of schizophrenia is defined by the presence of persistent and disabling symptoms of psychosis (delusions and hallucinations), disorganized speech or behavior, and negative symptoms, which include impoverishment in motivation, speech, and emotional expression. However, since the very earliest descriptions by Kraepelin, Huntingdon, & Robert (1971) and Bleuler (1950), significant and widespread problems in diverse areas of thinking skill, often referred to as *cognitive* or *neurocognitive* impairments, have also been identified. Overall, people with a schizophrenia diagnosis show a

wide range of general intellectual abilities, mirroring the distribution curve of the general population (although with a downward shift). But the vast majority do not achieve the expected level of development, based on usual predictive factors such as maternal IQ or education. Furthermore, most people with schizophrenia experience specific additional cognitive problems, with widely differing individual profiles, but typically in areas such as memory, concentration, problem solving, organization, planning, thinking speed, perceptual processing, or the understanding of social cues and situations. Studies of cohorts of people born within a certain timespan and within a defined geographical area show that:

- Cognitive difficulties are apparent in those who go on to develop schizophrenia before the specific symptoms emerge.
- Cognitive difficulties significantly worsen when symptoms emerge.
- With some fluctuations, these cognitive difficulties remain stable throughout life.

For individuals, common experiences resulting from cognitive difficulties include a significantly reduced concentration span, difficulties in remembering key personal past events or current information, or problems in thinking in an organized or strategic way. It seems self-evident that these experiences are likely to be detrimental to someone's quality of life, self-esteem, and personal identity. However, they are also known to be linked to limitations in the ability to achieve and maintain personal developmental milestones, in terms of employment, self-care, and social relationships. Thus, cognitive problems have emerged as a key treatment target in schizophrenia, particularly as a means to improving valued other outcomes, seen by patients as crucial for recovery.

Despite considerable recent interest in the field, there are currently no effective pharmacological treatments for cognitive problems in schizophrenia. There is, however, a psychological treatment, cognitive remediation, for which there is now a large body of evidence showing its benefits for both cognitive and functional skills in people with schizophrenia. It was recently defined, in 2012, by a Cognitive Remediation Experts Workshop as "an intervention targeting cognitive deficits using scientific principles of learning with the ultimate goal of improving functional outcomes. Its effectiveness is enhanced when provided in a context (formal or informal) that provides support and opportunity for improving everyday functioning." It takes a wide variety of forms but, usually consists primarily of a collection of tasks or puzzles targeting particular thinking skills, which appear much like those that have frequently appeared in publically available "brain training" programs. Tasks are practiced repetitively, usually over a period of several

months, and frequently rely on errorless learning (so that a high degree of success is maintained) and scaffolding (which allows patients to work slightly above their current ability level). These tasks might be presented in pencil-and-paper format, or increasingly, on a computer. A therapist may or may not guide the work, which can be conducted individually or in a group format, and the therapy may be more or less embedded within a more comprehensive clinical intervention. The continuum of presentation may range from a patient being given a laptop on which to practice a range of exercises at home for payment, to daily attendance at a clinic in which cognitive remediation is offered individually and in groups as part of a personally tailored, recovery-focused rehabilitation package, delivered by highly trained psychological therapists or other mental health professionals.

Cognitive remediation is beginning to be considered for clinical guidance and has recently been endorsed by the Scottish Intercollegiate Guideline Network, the body which develops evidence-based clinical practice guidelines for the National Health Service in Scotland, for inclusion as a part of routine clinical care. This entry describes the foundational background research to its development and effectiveness; summarizes the cutting-edge research into delivery enhancements and the underlying mechanisms of change; and argues that the current priorities for cognitive remediation should be to establish an evidence-based model for therapy to ensure that the active ingredients are sufficiently specified to ensure widespread dissemination that is both cost-effective and maximizes clinical change.

FOUNDATIONAL RESEARCH

Originating in the field of brain injury, cognitive remediation for schizophrenia has taken many forms and is distinct in the piecemeal trajectory of its development. No single model or group of models of how cognitive skills may be improved, or how cognitive changes achieved in a clinic or laboratory might be generalised or “transferred” to everyday life, underlie the wide variety of cognitive remediation programs that are available. The therapy emerged in a context of pessimism within which cognitive problems were considered to be immutable traits, and researchers began with a modest goal of improving performance on specific psychological tests of brain function. Following some initial successful forays, more comprehensive programs of cognitive remediation have been developed, which can be broadly grouped into two categories.

The first is often referred to as *drill-and-practice* cognitive remediation. This approach is tied to the idea that throughout life the brain is able to adapt and change in both its function and structure in response to experience. This is known as *neuroplasticity* and for neuroplastic changes to take place and

persist, changes in behavior which promote them should be small and incremental and done in a highly repetitive and intensive way over a sustained period of time. Drill-and-practice-based approaches tend to isolate specific basic cognitive skills, such as discriminating between two auditory tones or remembering short chunks of information, and to encourage people to practice these skills in a highly repetitive way, often on a daily basis for a period of at least a few months.

An alternative cognitive remediation approach is “strategy-based” and involves teaching patients strategies for improving cognitive performance. Originally conceived as a compensatory approach in which new strategies were thought to support or replace the use of impaired cognitive skills, a more recent conception has been that it helps people to develop a more systematic general approach to tasks, which can also be applied to everyday living. Thus, a clear means of transfer from the clinic to community skills is specified and intrinsic to the learning. According to this notion, in principle, the types of cognitive goals are likely to be different from the basic thinking skills targeted in drill-and-practice approaches, so that memory and problem-solving, planning and organizational abilities (collectively known as *executive functions*) are key. For these cognitive skills, strategy use is a normal intrinsic part of thinking (and is known to be frequently impaired in schizophrenia)—not a compensatory approach to impaired skills.

Traditionally, “drill-and-practice-based” cognitive remediation and “strategy-based” cognitive remediation have been seen as competing approaches, but, in practice, there is a common consensus that all cognitive remediation programs should include a substantial drill-and-practice component that targets basic cognitive skills. What remains at issue is the means by which the process of generalization or “transfer” from the clinic to everyday life occurs, because it is well established that learning tends to be highly context-dependent. Proponents of strategy-based cognitive remediation suggest that transfer may be facilitated by the explicit strategic teaching of executive skills as an intrinsic part of the cognitive remediation. Proponents of drill-and-practice-based approaches also acknowledge the importance of generalization, but prioritize the persistent targeting of basic cognitive skills, with some suggestion that through the process of neuroplastic change, cognitive improvement may automatically feed-forward into everyday tasks in which the targeted cognitive skills are in use.

An additional particular type of cognitive remediation deserves special mention—social cognition interventions. *Social cognition* refers to the mental processes involved in perceiving, attending to, remembering, thinking about, and making sense of the social world. Social cognitive remediation makes these processes the target and, analogous to the drill-and-practice versus strategy-based approaches of mainstream cognitive remediation,

social cognitive remediation tends to be targeted either to a specific domain of social cognition (e.g., the interpretation of facial expressions of emotion) or to incorporate a wide range of social cognitive domains to create a more complex rehabilitative intervention.

There is now good evidence to show that cognitive remediation (including social cognitive remediation), regardless of treatment approach, is an effective way of improving cognitive skills in people with a diagnosis of schizophrenia. In a recent study, which analyzed data collated from 40 controlled cognitive remediation studies published before June 2009, collectively including more than 2000 participants, Wykes, Huddy, and others (2011) showed that cognitive remediation leads to durable cognitive improvements and benefits for wider functioning (employment, everyday living skills). There were smaller positive effects for symptoms. Importantly, these results persisted even when the methodological rigor of the studies was taken into account. It is not unusual in research for the size of the effect of a treatment to be reduced if only the studies which are conducted in a very rigorous manner are considered: This was not the case for the cognitive remediation research.

The effectiveness of social cognitive remediation has also been assessed in a recent meta-analytic study, conducted by Matthew Kurtz and Richardson (2012). Data from 19 controlled studies were analyzed, which collectively included almost 700 participants. Results showed significant benefits for recognizing emotions from faces and theory of mind (the ability to attribute mental states to oneself and others). But not all aspects of social cognition were improved.

In addition to the overall effectiveness of cognitive remediation, the Wykes, Huddy *et al.* (2011) meta-analysis investigated some of the treatment and patient characteristics that may have affected the treatment response. In terms of patient characteristics, age, gender, and whether or not cognitive impairments had been used as a criterion for including participants to the study did not have an impact. However, having fewer symptoms at the start of therapy predicted a better response to cognitive remediation, and studies which included only people who had a schizophrenia or a schizo-affective diagnosis showed greater effects of cognitive remediation than studies which included people with other diagnoses.

Many treatment characteristics including length of therapy and whether or not a computer was used had no impact on outcome. The authors also investigated the relative effectiveness of the drill-and-practice versus drill-plus-strategy approaches. The positive effects of cognitive remediation on cognition were similar for both types of therapy approach. However, the effects on real-world functioning were considerably better for people who had received cognitive remediation in the context of additional psychiatric

rehabilitation (such as supported employment), particularly those who had received drill-plus-strategy-based cognitive remediation. Although including only a few studies, this effect was very marked: if participants had received drill-plus-strategy cognitive remediation as well as some kind of adjunctive therapy, the outcome was twice as good as for those who had received drill-and-practice cognitive remediation. This suggests that strategy-based approaches may facilitate the process of the transfer of new cognitive skills into daily life, and as predicted from evidence that learning is frequently context dependent, purely drill-plus-practice approaches do not provide a mechanism by which new learning can generalize outside the learning context. This is with the proviso that cognitive remediation may provide a window of opportunity for people to make especially good use of other rehabilitation programs or opportunities for practicing skills in the community, and that without these opportunities translating learning from cognitive remediation to everyday life may be difficult. This may be particularly true for some people with a schizophrenia diagnosis who are often involved in few community activities and may have little social contact.

CUTTING-EDGE RESEARCH

WHICH TYPES OF COGNITIVE REMEDIATION WORK BEST?

Evidence from recent randomized controlled trials of cognitive remediation support the finding that drill-and-practice approaches, without any direct attempts to facilitate the transfer of learning to an everyday environment, lead to cognitive improvements (as measured by tests of thinking skill), but not changes in functioning in real-world social or community settings. Consequently, increasingly cognitive remediation is appearing either as a complex intervention including drill-plus-strategy-based approaches, aspects of social cognitive remediation, and real-world goals; or paired with an adjunctive additional treatment whose goal may be oriented more explicitly to general functioning. These treatment trials report success not only in improving cognitive test performance but also in delivering improvements in psychosocial outcomes. The results of a large, rigorous trial of a typical combination of treatments was reported by Bowie, McGurk, Mausbach, Patterson, and Harvey (2012) who compared (i) drill-plus-strategy cognitive remediation, (ii) functional skills training, and (iii) a combination of the cognitive remediation followed by functional skills training. Changes following each single mode treatment were specific to their targets: Cognition, but not social or functional competence improved after cognitive remediation; and social and functional competence, but not cognition improved after functional skills training. The combination treatment not only produced each type of change but, in addition, improvements in functional competence

(community or household activities, and work skills) were greater and more durable. A more novel pairing of treatments has been investigated by Richard Drake *et al.* (2014). They preceded cognitive behavioural therapy for psychosis (CBTp), a psychological therapy designed to treat the symptoms of psychosis, with either drill-plus-strategy-based cognitive remediation or a time-matched control therapy. Although at the end of receipt of CBTp, both groups (cognitive remediation and active control) had a similar level of symptoms, those who had previously received cognitive remediation had required significantly fewer sessions of CBTp to achieve that outcome.

These studies suggest that while we can achieve cognitive improvements using only drill-and-practice cognitive remediation approaches, the more ambitious goal of benefiting real-world function is facilitated by a strategy-based approach, and this response is significantly enhanced in the context of adjunctive rehabilitation or psychological therapy. Crucially, the combination of cognitive remediation and adjunctive therapy may do more than the sum of its parts. Cognitive remediation appears to facilitate an enhanced response for patients with a schizophrenia diagnosis to other interventions, so that outcomes are significantly boosted or the intervention duration can be reduced.

HOW DOES COGNITIVE REMEDIATION WORK?

How cognitive remediation works needs to be addressed using two different questions: (i) How does cognitive improvement occur, and (ii) how are these cognitive improvements transferred or generalized to other areas of functioning? The studies described in the previous section tell us something about the second of these: the mechanisms by which cognitive change may affect other areas of functioning. There is clearly no direct relationship between cognitive and functional change: If this were to be true, then any cognitive change would be automatically linked to real-world changes. However, we know that improvements in cognition known to be linked cross-sectionally to psychosocial outcomes, are not always followed by the related psychosocial changes, and that this may depend on (i) the *type* of cognitive change (so that some cognitive targets might better than others), (ii) the *amount* of cognitive change (so that cognitive change may need to reach a certain threshold such as normalized performance in order to impact functional outcomes), and (iii) the *context* of cognitive change (so that, for example, it may be only influential on functional outcomes when occurring within a cognitive remediation program, or embedded within wider rehabilitation, or the person is very motivated to change).

A few studies have investigated these issues. In terms of *types* of cognitive change, which appear to be associated with real-world improvements,

there is some consistency in the finding that executive function improvement is a frequent specific cognitive predictor of real-world improvement. *Executive functions* refer to higher order thinking skills used in processing novel or goal-directed activities, and include aspects such as strategy use, organization, planning and self-monitoring. These are all generally targets of strategy-based cognitive remediation, and so this fits with the suggestion that strategy-based approaches are needed to facilitate the generalization of learning in cognitive remediation to daily life. They are also closely allied to the concept of metacognition, which has been suggested as a possible moderator of the relationship between cognition and social functioning. The suggestion is that it is only when people are able to understand their own cognitive strengths and difficulties (metacognitive knowledge) and effectively monitor and regulate their own thinking (metacognitive processing) that they are able to transfer new cognitive skills to an everyday context. A recent study by Wykes and colleagues (2012) examined a number of complex models for the relationship between cognitive change and work outcomes, investigating the impact of both types and levels of cognitive change. They showed that of a number of cognitive measures that improved following remediation, only planning improvement was associated with improved work quality. Those who had poorer memory and/or better cognitive flexibility were more likely to make planning improvements.

The issue of the *amount* of cognitive change that is necessary to achieve functional change has emerged in a number of studies, but has been little investigated. In a few studies of cognitive remediation (e.g., by Silverstein & colleagues, 2005), little or no measurable cognitive change was apparent, despite functional changes emerging. Thus, the benefits of therapy may have been mediated through its nonspecific effects on other areas of functioning, such as self-esteem, or it may be that our traditional tests of cognitive function are not sensitive enough to detect certain types or minimal levels of cognitive change. On the other hand, some studies, including those by Wykes and colleagues have shown that only when cognitive change reached a certain level has a measurable impact on social functioning been observable. Our understanding of this issue is in its infancy.

The *context* of cognitive change calls into question what other factors might be necessary to mediate or moderate a relationship between cognitive change and functional outcomes. Other factors that have been investigated so far have included learning potential (or the extent to which someone has the capacity to learn from experience), social cognition, motivation, cognitive reserve (or protective cognitive resources derived from experience), and metacognition (thinking about thinking). Although this research is in the early stages, there is emerging evidence that motivation and social cognition may need to be boosted to maximize cognitive improvements are to take

place and to be transferred to everyday living. Both these factors are very frequently reduced or impaired in people with schizophrenia. Motivation may be a particularly crucial factor to explore further, because massed practice is so important for cognitive remediation: Patients need to complete sessions daily over several months. Generally, cognitive remediation programs have either involved a therapist to offer social reinforcement and to ensure the intervention is tailored to an individual's needs and goals or they have offered monetary rewards. Both these methods have cost implications for the delivery of cognitive remediation, but there are also ethical issues arising from payment of patients. But the relative merits of either approach or their effects on either motivation or learning have not been investigated.

Studies have also begun to investigate biological correlates of cognitive improvement, which offer the potential to identify more sensitively the process of change. Early brain imaging studies showed increased activation following cognitive remediation in areas of the brain known to be frequently underactive in schizophrenia and associated with cognitive or social cognitive impairment (e.g., the frontal lobe for cognitive function, or recently, in one study the postcentral gyrus for emotion recognition). More recently, a study of brain morphology by Eack and colleagues (2010) showed that 2 years of a comprehensive and broad-ranging cognitive remediation program provided to people early in the course of a schizophrenia diagnosis, provided a neuroprotective effect. People who had received cognitive remediation showed preserved or even increased gray matter compared to those who had received an enriched supportive therapy. This is consistent with the proposition that cognitive remediation facilitates neuroplastic changes in the brain and has led to the suggestion that cognitive remediation may best be targeted at young people with a diagnosis of schizophrenia, when neuroplasticity potential may be greatest and to protect against future neurobiological decline.

The application of cognitive remediation to specific subgroups of the population, such as those early in the course of the disorder, is another cutting-edge development in the field. Studies of cognitive remediation with young people, even those at high risk of developing psychosis, rather than those with established symptoms, are increasing although there are difficulties in recruitment as individuals who do not yet have a diagnosis are less engaged with services.

KEY ISSUES FOR FUTURE RESEARCH

A consensus regarding the importance of some elements of cognitive remediation, including massed practice, strategy-based learning to facilitate transfer, and enhanced motivation, is beginning to emerge. However, to

allow widespread dissemination, we need to optimize effectiveness while continuing to be cost-effective and this is most likely to be achieved by generating a unifying model of change. Any such model needs to address two related questions: (i) How can we optimize cognitive improvement, and (ii) how can cognitive change best be transferred to everyday life? It is apparent that there are currently two predominant levels of explanation emerging in response to these questions, one based on cognitive psychology and the other on neuroscience. Cognitive levels of explanation for how cognition is improved have tended to refer to the development of new mental models or “schemas” that may become automatized over time, while the prevailing neuroscientific explanations emphasize the importance of brain adaptations or neuroplastic changes to compensate for impaired or declining processes. Cognitive-level explanations have also primarily been offered for the transfer process from cognitive learning to everyday living skills, emphasizing the development of metacognitive or social cognitive strategic processing to help people learn how to use new or existing cognitive skills to improve performance across a wide variety of domains. Neuroscience has suggested that new brain functions may be automatically recruited in new situations or that there may be an automatic feed-forward of change from one area of cognitive function to another. Both levels of explanation need to be developed, and compared or linked, if we are to understand change more comprehensively.

In relation to understanding the process of change, we need to consider the role of other factors that may mediate or moderate cognitive change and its transfer to functional outcomes. In particular, we need to identify patient and therapy characteristics. Patient characteristics may not only help target treatments more effectively but also aid our understanding of the intrapersonal processes involved in change. Therapy characteristics will allow us to identify active ingredients, which can in turn be used to provide insight into the types of interpersonal, cognitive, or brain processes that may facilitate change. In relation to these, patient characteristics that appear to hold promise in elucidating change are age and cognitive reserve (measured using behavioral neuropsychological assessment and brain imaging methods).

One therapy characteristic which still deserves attention is the long-standing difference between the drill-and-practice versus strategy-based approaches. It is not clear whether the addition of an optimal strategy-based approach to drill-and-practice training within cognitive remediation can be *sufficient* to promote transfer to daily living skills, whether a strategy focus is *necessary* to facilitate transfer for drill-and-practice approaches, or whether some kind of additional adjunctive therapy is always necessary for generalization to take place.

In addition, with the increasing need to create a cost-effective, easily disseminated version of cognitive remediation, the therapy is being transferred to computers, minimizing the need for a therapist. What is not clear is the extent to which a therapist is important in facilitating change and other related factors, such as engagement and motivation, and how much a patient can gain from working alone, with or without monetary incentives. In relation to this, and of importance in considering more widespread adoption of cognitive remediation into clinical services, is the level of training required for clinicians offering cognitive remediation to therapists and whether this is best done by psychologists or other mental health professionals.

Finally, one promising area of new research is in the interaction of cognitive remediation with biological factors such as medication use and genes, which may enhance response to help us to identify and target groups of people with a schizophrenia diagnosis who may benefit from different approaches. These may provide yet another neurobiological level of explanation for the process of cognitive and concomitant changes. Medication might also allow us to remove the rate limiter on neuroplastic change, particularly in older clients, thus allowing for further effects of cognitive remediation as synergistic treatments.

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